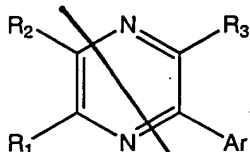


WHAT IS CLAIMED IS:

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

Ar is substituted phenyl, optionally substituted naphthyl, or an optionally substituted heterocyclic group having from 1 to 3 rings, and 3 to 8 ring members in each ring and 1 to about 3 hetero atoms;

- 10 R₁ and R₃ are each independently hydrogen, halogen, cyano, nitro, amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted mono or dialkylamino, optionally substituted alkoxy, optionally substituted alkylthio, optionally substituted alkylsulfinyl, or optionally substituted alkylsulfonyl; and

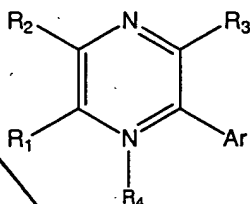
- 15 R₂ is halogen, cyano, nitro, amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkylamino, optionally substituted alkoxy, optionally substituted alkylthio, optionally substituted alkylsulfinyl, or optionally substituted alkylsulfonyl;

- 20 with the proviso that if Ar is phenyl substituted with halogen, naphthyl, or naphthyl substituted with halogen, then the compounds where R₃ is hydrogen or amino are excluded.

2. A compound according to Claim 1, wherein:

- Ar is substituted phenyl, optionally substituted naphthyl, or an optionally substituted
25 heterocyclic group having at least one nitrogen ring atom or at least one sulfur ring atom.

- sub C2*
3. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

R₁ is selected from H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, halogen, CN, C₁₋₄ haloalkyl, trifluoromethyl, trifluoromethoxy, -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), -O(C₁₋₄ alkyl), and S(O)_n(C₁₋₄ alkyl);

R₂ is selected from the group consisting of -XR_A and Y, wherein -X, R_A, and Y are defined below; and

R₃ is selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), and -S(O)_n(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, trifluoromethoxy, -XR_A and Y;

R₄ is absent or an oxygen atom;

Ar is phenyl, mono-, di-, or tri-substituted with R_C, or

Ar is selected from the group consisting of:

naphthyl, pyridyl, pyridonyl, pyrimidinyl, and thiophenyl, each of which is unsubstituted or mono-, di-, or tri-substituted with R_C;

with the proviso that if Ar is phenyl substituted with halogen, naphthyl, or naphthyl substituted with halogen, then the compounds where R₃ is hydrogen are excluded;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of: hydrogen and straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) selected from oxo, hydroxy, halogen, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), -NHC(O)(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)C(=O)(C₁₋₄ alkyl), -NHS(O)_n(C₁₋₄ alkyl), -S(O)_n(C₁₋₄ alkyl), -S(O)_nNH(C₁₋₄ alkyl), -S(O)_nN(C₁₋₄ alkyl)(C₁₋₄ alkyl), and Z;

R_C is independently selected at each occurrence from the group consisting of halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆

C2
cont

5 alkyl optionally substituted with 0-2 R_D , C_{2-6} alkenyl substituted with 0-2 R_D , C_{1-4} alkynyl substituted with 0-2 R_D , C_{3-7} cycloalkyl substituted with 0-2 R_D , (C_{3-7} cycloalkyl) C_{1-4} alkyl substituted with 0-2 R_D , $-O(C_{1-4}$ alkyl) substituted with 0-2 R_D , $-NH(C_{1-4}$ alkyl) substituted with 0-2 R_D , $-N(C_{1-4}$ alkyl)(C_{1-4} alkyl) each independently substituted with 0-2 R_D , $-XR_A$, and Y;

R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C_{1-4} alkyl, $-O(C_{1-4}$ alkyl), $-NH(C_{1-4}$ alkyl), $-N(C_{1-4}$ alkyl)(C_{1-4} alkyl), morpholino, pyrrolidino, piperidino, thiomorpholino, piperazino, 4-hydroxypiperidino, $-S(O)_n(C_{1-4}$ alkyl), trifluoromethyl, trifluoromethoxy, $CO(C_{1-4}$ alkyl), $CONH(C_{1-4}$ alkyl), $CON(C_{1-4}$ alkyl)(C_{1-4} alkyl), $-XR_A$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_B-$, $-O-$, $-C(=O)-$, $-C(=O)O-$, $-S(O)_n-$, $-NH-$, $-NR_B-$, $-C(=O)NH-$, $-C(=O)NR_B-$, $-S(O)_nNH-$, $-S(O)_nNR_B-$, $-OC(=S)S-$, $-NHC(=O)-$, $-NR_BC(=O)-$, $-NHS(O)_n-$, $-OSiH_n(C_{1-4}alkyl)_{2-n}-$, and $-NR_BS(O)_n-$; and

15 Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents selected from halogen, haloalkyl, oxo, hydroxy, amino, C_{1-4} alkyl, $-O(C_{1-4}$ alkyl), $-NH(C_{1-4}$ alkyl), $-N(C_{1-4}$ alkyl)(C_{1-4} alkyl), and $-S(O)_n(C_{1-4}$ alkyl), and
20 said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen; and

n is independently selected at each occurrence from 0, 1, and 2.

25
B1

4. A compound of according to Claim 1 wherein Ar is substituted phenyl.

5. A compound according to Claim 3, R_4 is absent and Ar is phenyl, mono-, di-, or tri-substituted with R_C .

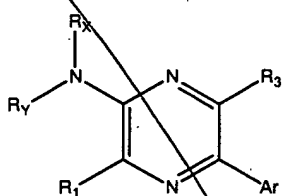
6. A compound according to Claim 3 wherein R_4 is absent and Ar is phenyl, mono-, di-, or tri-substituted with R_C , and R_1 and R_3 are independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, ethoxy and methoxy.

5 *D1 cont* 7. A compound according to Claim 3 wherein R_4 is absent and Ar is phenyl, mono-, di-, or tri-substituted with R_C ; and R_A and R_B , which may be the same or different, are independently straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds.

10 8. A compound according to Claim 3 wherein R_4 is absent and Ar is phenyl mono-, di-, or tri-substituted with R_C ; R_A and R_B , which may be the same or different, are independently selected at each occurrence from the group consisting of: straight, branched, and cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds; and

15 R_1 and R_3 are independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, ethoxy, and methoxy.

Sub a1 9. A compound of the Formula:



20 Formula A

wherein

R_X and R_Y are the same or different and are independently selected straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) independently selected from hydroxy, halogen, $-O(C_{1-4} \text{ alkyl})$, $-NH(C_{1-4} \text{ alkyl})$, $-N(C_{1-4} \text{ alkyl})(C_{1-4} \text{ alkyl})$, and optionally substituted phenyl.

10. A compound according to Claim 9, wherein Ar is phenyl, mono-, di-, or tri-substituted with R_C; and R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, ethoxy and methoxy.

5 11. A compound according to Claim 9, wherein:

R₁ and R₃ are independently chosen from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy; and

10 Ar is phenyl, which is mono-, di-, or trisubstituted with one or more substituent(s) independently selected from:

halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.

15 12. A compound according to Claim 9, wherein:

R_X is hydrogen;

R_Y is chosen from the group consisting of:

straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds;

20 R₁ and R₃ are independently chosen from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy; and

Ar is phenyl, which is mono-, di-, or trisubstituted with substituent(s) independently selected from:

25 halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.

13. A compound according to Claim 9, wherein:

30 R_X is hydrogen;

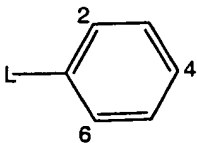
DI cont

~~R_Y is chosen from the group consisting of:~~

~~straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds;~~

~~R₁ and R₃ are independently chosen from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy; and~~

~~Ar is a phenyl group of the formula:~~



~~wherein L indicates a bond to the pyrazine ring in Formula A;~~

~~and the phenyl group is substituted at one, two or three of positions 2, 4, and 6 with substituent(s) independently selected from:~~

~~halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.~~

14. A compound according to Claim 9, wherein:

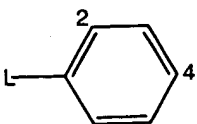
R_X is hydrogen;

R_Y is chosen from the group consisting of:

straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds;

R₁ and R₃ are independently chosen from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy; and

Ar is a phenyl group of the formula:

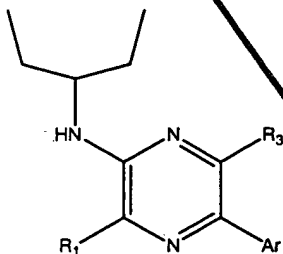


wherein L indicates a bond to the pyrazine ring in Formula A;

and the phenyl group is substituted at positions 2 and 4 with substituents independently selected from:

halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.

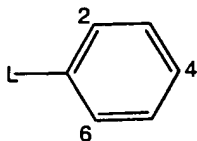
15. A compound according to Claim 9 of the formula:



wherein:

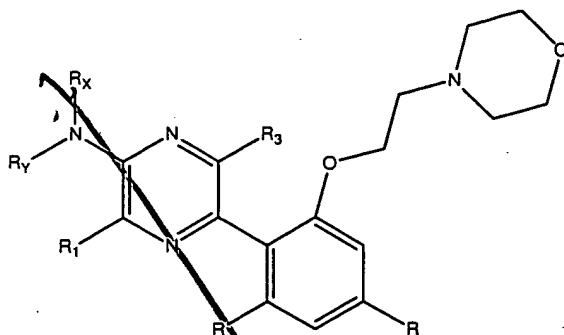
- 10 R₁ and R₃ are independently chosen at each occurrence from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy; and

Ar is a phenyl group of the formula:



- 15 wherein L indicates a bond to the pyrazine ring in Formula A;
and the phenyl group is substituted at one, two or three of positions 2, 4, and 6 with substituent(s) independently selected from:
halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.
- 20

16. A compound according to Claim 9 of the formula:



wherein

R is independently selected at each occurrence from the group consisting of: hydrogen, halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C₁₋₆alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino; and

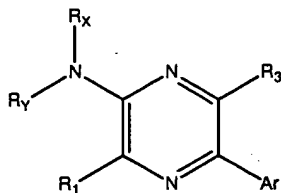
R₁ and R₃ are independently chosen from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy.

17. A compound according to Claim 9 wherein Ar is phenyl, which is mono-, di-, or tri-substituted with R_C;

R_X and R_Y, which may be the same or different, are independently selected at each occurrence from the group consisting of: straight, branched, and cyclic alkyl groups having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds; and

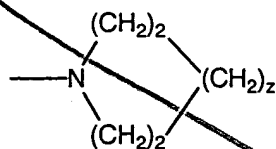
R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, ethoxy, and methoxy.

18. A compound according to Claim 3 of the formula:



wherein R_X and R_Y are independently hydrogen or C₁₋₈ alkyl; or

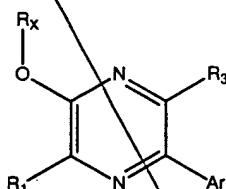
NR_XR_Y is:



wherein z is 0 or 1.

Sub A2

19. A compound of the Formula:



Formula B

wherein:

R_X is chosen from the group consisting of:

straight, branched, or cyclic alkyl groups, including (cycloalkyl)alkyl groups, having from 1 to 8 carbon atoms, which may contain one or more double or triple bonds, each of which may be further substituted with one or more substituent(s) independently selected from

(a) hydroxy, halogen, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), and

(b) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents selected from halogen, haloalkyl, oxo, hydroxy, amino, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)(C₁₋₄ alkyl) and wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

BOOK REVIEW

DI
cont

5

10

halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, and C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.

15

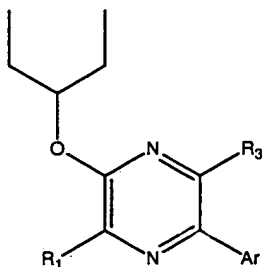
20

25

- 175 -

and the phenyl group is substituted at positions 2 and 4 with substituents independently selected from halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.

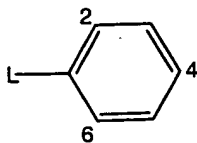
23. A compound according to Claim 19, of the formula:



wherein:

R₁ and R₃ are independently chosen from halogen, C₁₋₄ alkyl, -O(C₁₋₄ alkyl), -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)(C₁₋₄ alkyl), haloalkyl, trifluoromethyl, and trifluoromethoxy; and

Ar is a phenyl group of the formula:

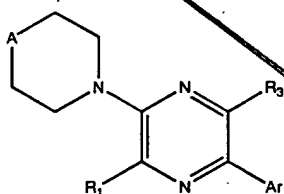


wherein L indicates a bond to the pyrazine ring in Formula B;

and the phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituent(s) independently selected from: halogen, cyano, haloalkyl, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄alkoxy), mono- or di(C₁₋₄)amino(C₁₋₄alkoxy), and mono- or di(C₁₋₄ alkyl)amino.

24. A compound according to Claim 19 wherein R₁ and R₃ are independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, ethoxy and methoxy.

25. A compound according to Claim 3 of the formula:



wherein A is NR_A or O.

5

26. A compound according to Claim 1 wherein, in a standard in vitro CRF receptor binding assay the compound exhibits an IC₅₀ value less than or equal to 1 micromolar.

10

27. A method for modulating CRF receptor function, comprising administering to a patient in need of such modulation an effective amount of a compound of according to Claim 1.

15

28. A method for treating a CNS disorder or disease, comprising administering to a patient in need of such treatment an effective amount of a compound according to Claim 1.

20

29. The method of Claim 28 wherein the CNS disorder or disease is an anxiety disorder, stress-related disorder, or eating disorder.

DI
cont

30. A compound according to Claim 1, wherein in a standard in vitro sodium channel functional assay the compound does not show any statistically significant activity at the $p < 0.05$ level of significance.

25

31. A method of Claim 28 wherein the CNS disease or disorder is depression or a bipolar disorder.

32. A method of Claim 28 wherein the CNS disease or disorder is anorexia nervosa, bulimia nervosa, or obesity.

33. A method according to Claim 28 wherein in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 1 micromolar.

34. A method according to Claim 28 wherein in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 100 nanomolar.

35. A method according to Claim 28 wherein in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 10 nanomolar.

36. A method according to Claim 28 wherein the patient is a human.

37. A method for localizing CRF receptors in tissue section samples comprising:

contacting with a sample of tissue a detectably-labelled compound of Claim 1 under conditions that permit binding of the compound to CRF receptors within the sample of tissue;

washing the tissue sample to remove unbound compound; and

detecting remaining bound compound.

38. A method of inhibiting the binding of CRF to a CRF1 Receptor which comprises:

contacting a solution comprising CRF and a compound of Claim 3 with a cell the receptor, wherein the compound is present in the solution at a concentration sufficient to inhibit CRF binding to IMR32 cells in vitro.

39. A method for altering the signal-transducing activity of a CRF1 receptor, the method comprising contacting cells expressing the receptor with a compound according to Claim 3.

40. A method of modulating G-protein coupled receptor function, the method comprising exposing cells expressing a G-protein coupled receptor to an effective amount of a compound according to Claim 3.

41. A method according to Claim 40, wherein the G-coupled protein receptor is a CRF1 receptor.

42. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to Claim 1.

43. A packaged pharmaceutical composition comprising a pharmaceutical composition of claim 42 in a container and instructions for using the composition to treat a patient suffering from an anxiety disorder, a stress-related disorder, or an eating disorder.

44. A compound according to Claim 3, named 5-(2,4-dimethoxyphenyl)-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

45. A compound according to Claim 3, named 5-[4-bromo-2-(trifluoromethoxy)phenyl]-3,6-diethyl-N-(1-ethylpropyl)pyrazin-2-amine.

46. A compound according to Claim 3, named 3-ethyl-N-(1-ethylpropyl)-6-methoxy-5-[2-methoxy-4-(trifluoromethoxy)phenyl] pyrazin-2-amine.

47. A compound according to Claim 3, named 5-(4-chloro-2-methylphenyl)-6-

ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

48. A compound according to Claim 3, named 5-[2-chloro-4-(trifluoromethyl)phenyl]-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

49. A compound according to Claim 3, named 2-[2,4-bis(trifluoromethyl)phenyl]-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

50. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-naphthyl)pyrazin-2-amine.

51. A compound according to Claim 3, named 5-[4-chloro-2-(trifluoromethyl)phenyl]-3,6-diethyl-N-(1-ethylpropyl)pyrazin-2-amine.

52. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-[2-methoxy-6-(trifluoromethoxy)phenyl]pyrazin-2-amine.

53. A compound according to Claim 3, named 5-(2-chloro-4-methoxyphenyl)-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

54. A compound according to Claim 3, named 5-(2,6-dichloro-4-methoxyphenyl)-3,6-diethyl-N-(1-ethylpropyl)pyrazin-2-amine.

55. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(3-methyl-1,1'-biphenyl-4-yl)pyrazin-2-amine.

56. A compound according to Claim 3, named 5-[2,4-bis(trifluoromethyl)phenyl]-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

57. A compound according to Claim 3, named 2-(2,4-dichlorophenyl)-3,6-

outside 7
3 case

diethyl 5-(1-methylbutoxy)pyrazine.

58. A compound according to Claim 3, named 2,5-diethyl-3-(1-isopropyl-2-methylpropoxy)-6-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrazine.

59. A compound according to Claim 3, named 2,5-diethyl-3-(1-isopropyl-2-methylpropoxy)-6-[2-methyl-4-(trifluoromethoxy)phenyl]pyrazine.

60. A compound according to Claim 3, named 5-[4-chloro-2-(trifluoromethyl)phenyl]-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

61. A compound according to Claim 3, named N-(1-ethylpropyl)-3-methoxy-5-[2-methoxy-4-(trifluoromethoxy)phenyl]-6-methylpyrazin-2-amine.

62. A compound according to Claim 3, named 5-[4-chloro-2-(trifluoromethyl)phenyl]-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

63. A compound according to Claim 3, named 3-ethyl-N-(1-ethylpropyl)-6-methoxy-5-[2-methyl-4-(trifluoromethoxy)phenyl]pyrazin-2-amine.

64. A compound according to Claim 3, named 5-(2,4-dimethylphenyl)-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

65. A compound according to Claim 3, named 5-(2-chloro-4-ethoxyphenyl)-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

66. A compound according to Claim 3, named O-(3-chloro-4-{5-[(1-ethylpropyl)amino]-6-methoxy-3-methylpyrazin-2-yl}phenyl) S-propyl (dithiocarbonate).

67. A compound according to Claim 3, named 2,5-diethyl-3-(1-ethylpropoxy)-

6-[2-methoxy-4,6-bis(trifluoromethyl)phenyl]pyrazine.

DI
cont 5 68. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(4-fluoro-2-methoxyphenyl)pyrazin-2-amine.

69. A compound according to Claim 3, named 5-(2-chloro-4-methylphenyl)-3,6-diethyl-N-(1-ethylpropyl)pyrazin-2-amine.

10 70. A compound according to Claim 3, named 5-(4-chloro-2-methoxyphenyl)-3,6-diethyl-N-(1-ethylpropyl)pyrazin-2-amine.

71. A compound according to Claim 3, named O-(3-chloro-4-{3,6-diethyl-5-[(1-ethylpropyl)amino]pyrazin-2-yl}phenyl) S-propyl (dithiocarbonate).

15 72. A compound according to Claim 3, named 5-(4-chloro-2,6-dimethoxyphenyl)-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

20 73. A compound according to Claim 3, named 2-(2,4-dimethoxyphenyl)-3,6-diethyl-5-(1-ethylbutoxy)pyrazine.

74. A compound according to Claim 3, named 5-[4-(1,3-dioxolan-2-yl)-2,6-dimethoxyphenyl]-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

25 75. A compound according to Claim 3, named 5-(4-ethoxy-2-methoxyphenyl)-3-ethyl-N-(1-ethylpropyl)-6-methoxypyrazin-2-amine.

76. A compound according to Claim 3, named 6-ethyl-N-(1-ethylpropyl)-3-methoxy-5-(2-methoxy-6-methylphenyl)pyrazin-2-amine.

30 77. A compound according to Claim 3, named 2-(2-chloro-4-methoxyphenyl)-

3,6-diethyl-5-(1-isopropyl-2-methylpropoxy)pyrazine.

78. A compound according to Claim 3, named 2-(4-{5-[(1-ethylpropyl)amino]-6-methoxy-3-methylpyrazin-2-yl}-3,5-dimethoxyphenyl)propan-2-ol.

79. A compound according to Claim 3, named 5-(4-chloro-2-ethoxyphenyl)-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

80. A compound according to Claim 3, named 3-ethyl-5-(2-ethyl-4-methoxyphenyl)-N-(1-ethylpropyl)-6-methoxypyrazin-2-amine.

81. A compound according to Claim 3, named 5-(4-chloro-2-ethoxyphenyl)-3-ethyl-N-(1-ethylpropyl)-6-methoxypyrazin-2-amine.

82. A compound according to Claim 3, named 5-(2-chloro-4-isopropoxyphenyl)-3-ethyl-N-(1-ethylpropyl)-6-methoxypyrazin-2-amine.

83. A compound according to Claim 3, named 5-[2-chloro-4-(1-ethylpropoxy)phenyl]-6-ethyl-N-(1-ethylpropyl)-3-methoxypyrazin-2-amine.

84. A compound according to Claim 3, named 5-[2-chloro-4-(1-ethylpropoxy)phenyl]-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

85. A compound according to Claim 3, named 5-(2,4-dichlorophenyl)-N-(1-ethylpropyl)-6-methoxy-3-methylpyrazin-2-amine.

86. A compound according to Claim 3, named 5-[2'-chloro-4',5'-bis(trifluoromethyl)-1,1'-biphenyl-2-yl]-N-(1-ethylpropyl)-6-methoxy-3-methylpyrazin-2-amine.

D1
cont

87. A compound according to Claim 3, named N-(1-ethylpropyl)-5-(4-fluoro-2-methoxyphenyl)-6-methoxy-3-methylpyrazin-2-amine.

5 88. A compound according to Claim 3, named 5-(2,4-dimethylphenyl)-N-(1-ethylpropyl)-6-methoxy-3-methylpyrazin-2-amine.

89. A compound according to Claim 3, named 2,5-diethyl-3-(2-ethyl-4-methoxyphenyl)-6-(1-isopropyl-2-methylpropoxy)pyrazine.

10 90. A compound according to Claim 3, named 5-(4-ethoxy-2-isopropoxyphenyl)-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

15 91. A compound according to Claim 3, named 5-[2-chloro-4-(1-ethylpropoxy)phenyl]-3-ethyl-N-(1-ethylpropyl)-6-methoxypyrazin-2-amine.

92. A compound according to Claim 3, named 2-[2-chloro-4-(trifluoromethyl)phenyl]-3,6-diethyl-5-(1-ethylbutoxy)pyrazine.

20 93. A compound according to Claim 3, named N-(1-ethylpropyl)-5-[4-(1-fluoroethyl)-2,6-dimethoxyphenyl]-3-methoxy-6-methylpyrazin-2-amine.

94. A compound according to Claim 3, named 5-[2-chloro-4-(2-methoxyethoxy)phenyl]-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

25 95. A compound according to Claim 3, named 5-[4-(difluoromethoxy)-2-methoxyphenyl]-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

30 96. A compound according to Claim 3, named 5-{2-[(dimethylamino)methyl]-4-methoxyphenyl}-N-(1-ethylpropyl)-3-methoxy-6-methylpyrazin-2-amine.

97. A compound according to Claim 3, named (2-{5-[(1-ethylpropyl)amino]-6-methoxy-3-methylpyrazin-2-yl}-5-methoxyphenyl)methanol.

5 98. A compound according to Claim 3, named 5-[4-(difluoromethoxy)-2-methoxyphenyl]-3-ethyl-N-(1-ethylpropyl)-6-methoxypyrazin-2-amine.

99. A compound according to Claim 3, named 2-(2-chloro-4-propoxyphenyl)-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

10 100. A compound according to Claim 3, named 2-[2-chloro-4-(cyclopropylmethoxy)phenyl]-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

15 101. A compound according to Claim 3, named 2-[2-chloro-4-(2-fluoroethoxy)phenyl]-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

102. A compound according to Claim 3, named N-(1-ethylpropyl)-5-(4-isopropoxy-2-methoxyphenyl)-3-methoxy-6-methylpyrazin-2-amine.

20 103. A compound according to Claim 3, named 2-(4-{[tert-butyl(dimethyl)silyl]oxy}-2-isopropoxyphenyl)-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

104. A compound according to Claim 3, named 2-(4-ethoxy-2-methoxyphenyl)-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

25 105. A compound according to Claim 3, named 2-(2,6-dimethoxyphenyl)-3,6-diethyl-5-(1-ethylbutoxy)pyrazine.

30 106. A compound according to Claim 3, named 4-{3-ethyl-5-[(1-ethylpropyl)amino]-6-methoxypyrazin-2-yl}-3-methoxyphenol.

D'
cont

107. A compound according to Claim 3, named 6-ethyl-N-(1-ethylpropyl)-5-(4-isopropoxy-2-methoxyphenyl)-3-methoxypyrazin-2-amine.

5 108. A compound according to Claim 3, named 4-[3,6-diethyl-5-(1-isopropyl-2-methylpropoxy)pyrazin-2-yl]-3-ethylphenol.

109. A compound according to Claim 3, named 3-ethyl-N-(1-ethylpropyl)-5-[4-fluoro-2-(trifluoromethyl)phenyl]-6-methoxypyrazin-2-amine.

10 110. A compound according to Claim 3, named 2,5-diethyl-3-(1-isopropyl-2-methylpropoxy)-6-mesitylpyrazine.

15 111. A compound according to Claim 3, named 2,5-diethyl-3-(1-ethylpropoxy)-6-(4-methoxy-2-methylphenyl)pyrazine.

112. A compound according to Claim 3, named 2,5-diethyl-3-[4-methoxy-2-(trifluoromethoxy)phenyl]-6-(1-propylbutoxy)pyrazine.

20 113. A compound according to Claim 3, named 6-chloro-5-[2-methoxy-4-(trifluoromethoxy)phenyl]pyrazin-2-amine.

114. A compound according to Claim 3, named 2-(4-butoxy-2-chlorophenyl)-3,6-diethyl-5-(1-ethylbutoxy)pyrazine.

25 115. A compound according to Claim 3, named 3-bromo-N-(1-ethylpropyl)-6-methoxy-5-[2-methoxy-4-(trifluoromethoxy)phenyl]pyrazin-2-amine.

30 116. A compound according to Claim 3, named 2-(4-{[tert-butyl(dimethyl)silyl]oxy}-2-ethoxyphenyl)-3,6-diethyl-5-(1-ethylpropoxy)pyrazine.

117. A compound according to Claim 3, named 6-methoxy-5-[2-methoxy-4-(trifluoromethoxy)phenyl]pyrazin-2-ylformamide.

118. A compound according to Claim 3, named 2,5-diethyl-3-(2-ethylbutyl)-6-[2-methoxy-4-(trifluoromethoxy)phenyl]pyrazine.

119. A compound according to Claim 3, named 2,5-diethyl-3-(1-ethylpropoxy)-6-(2-isopropoxy-4-propoxyphenyl)pyrazine.

120. A compound according to Claim 3, named 2-(sec-butylthio)-5-(2,4-dimethoxyphenyl)-3,6-diethylpyrazine.

121. A compound according to Claim 3, named 5-(4-chloro-2,6-dimethoxyphenyl)-6-methoxypyrazin-2-amine.

122. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-methyl-4-chlorophenyl)pyrazin-2-amine.

123. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-methyl-4-fluorophenyl)pyrazin-2-amine.

124. A compound according to Claim 3, named 3,6-diethyl-N,N-(2-methoxyethyl)-5-(2,4-dichlorophenyl)pyrazin-2-amine.

125. A compound according to Claim 3, named 3,6-diethyl-N-propyl-N-(cyclopropylmethyl)-5-(2,4-dichlorophenyl)pyrazin-2-amine.

126. A compound according to Claim 3, named 3,6-diethyl-2-(1-ethylpropoxy)-5-(2-methoxy-4,6-dimethylphenyl)pyrazine.

127. A compound according to Claim 3, named 3,6-dimethyl-2-(1-ethylpropoxy)-5-(2,4-dichlorophenyl)pyrazine.

128. A compound according to Claim 3, named 3,6-diethyl-2-(1-ethylpropoxy)-5-(2-hydroxy-4,6-dimethylphenyl)pyrazine.

129. A compound according to Claim 3, named 3,6-diethyl-2-(1-ethylpropoxy)-5-(2,4-dichlorophenyl)pyrazine.

130. A compound according to Claim 3, named 3,6-dimethyl-N-(1-methoxy-2-butyl)-5-(2,4-dimethoxyphenyl) pyrazin-2-amine.

131. A compound according to Claim 3, named 2-(2,4-dichlorophenyl)-5-[2-(methoxymethyl)pyrrolidin-1-yl]-3,6-dimethylpyrazine.

132. A compound according to Claim 3, named 2-(2,4-dimethoxyphenyl)-5-[2-(methoxymethyl) pyrrolidin-1-yl]-3,6-dimethylpyrazine.

133. A compound according to Claim 3, named 3,6-dimethyl-N-(1-ethylpropyl)-5-(2-methyl-4-chlorophenyl)pyrazin-2-amine.

134. A compound according to Claim 3, named 3,6-dimethyl-N-(1-ethylpropyl)-5-(2-trifluoromethyl-4-dimethylaminophenyl)pyrazin-2-amine.

135. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-trifluoromethoxy-4-methoxyphenyl)pyrazin-2-amine.

136. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-methoxy-4-trifluoromethylphenyl)pyrazin-2-amine.

137. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-trifluoromethyl-4-methoxyphenyl)pyrazin-2-amine.

138. A compound according to Claim 3, named 3,6-diethyl-N-(1-ethylpropyl)-5-(2-methoxy-4-methylphenyl)pyrazin-2-amine.

139. A compound according to Claim 3, named 3,6-diethyl-N-(1-methoxy-2-butyl)-5-(2-chloro-4-dimethylaminophenyl)pyrazin-2-amine.

10 140. A compound according to Claim 3, named 3,6-diethyl-N-(1-methylpropyl)-5-(2-chloro-4-dimethylaminophenyl)pyrazin-2-amine.

141. A compound according to Claim 3, named 3,6-diethyl-N-(2-methylpropyl)-5-(2-chloro-4-dimethylaminophenyl)pyrazin-2-amine.

15 142. A compound according to Claim 3, named 3,6-diethyl-N-(2-phenylethyl)-5-(2-chloro-4-dimethylphenyl)pyrazin-2-amine.

20 143. A compound according to Claim 3, named 3,6-diethyl-N-(1-propylbutyl)-5-(2-trifluoromethyl-4-dimethylaminophenyl)pyrazin-2-amine.

144. A compound according to Claim 3, named 3,6-diethyl-N-(1-methoxy-2-butyl)-5-(2-trifluoromethyl-4-dimethylaminophenyl)pyrazin-2-amine.

25 145. A compound according to Claim 3, named 2-(2,6-dimethoxy-4-chlorophenyl)-6-ethyl-5-(1-ethylpropoxy)-3-methoxypyrazine.

146. A compound named 2-(2-methoxy-5-trifluoromethoxyphenyl)-3-ethyl-6-methylamino-5-(1-ethylpropoxy)-pyrazine.

147. A method for treating a CNS disorder or disease, comprising administering to a patient in need of such treatment between 0.1 to 140 mg per kg body weight per day of a compound according to Claim 3.

5 148. The method of Claim 147 wherein the CNS disorder or disease is an anxiety disorder, stress-related disorder, or eating disorder.

149. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of a compound according to Claim 3.

10

150. A compound according to Claim 3 wherein, in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 1 micromolar.

15 151. A method for modulating CRF receptor function, comprising administering to a patient in need of such modulation an effective amount of a compound of according to Claim 3.

20 152. A method for treating a CNS disorder or disease, comprising administering to a patient in need of such treatment an effective amount of a compound according to Claim 3.

153. The method of Claim 152 wherein the CNS disorder or disease is an anxiety disorder, stress-related disorder, or eating disorder.

25

154. A compound according to Claim 3, wherein in a standard in vitro sodium channel functional assay the compound does not show any statistically significant activity at the $p < 0.05$ level of significance.

D1
cont

155. A method of Claim 152 wherein the CNS disease or disorder is depression or a bipolar disorder.

156. A method of Claim 152 wherein the CNS disease or disorder is anorexia nervosa, bulimia nervosa, or obesity.

157. A method according to Claim 152 wherein in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 1 micromolar.

158. A method according to Claim 152 wherein in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 100 nanomolar.

159. A method according to Claim 152 wherein in a standard in vitro CRF receptor binding assay the compound exhibits an IC_{50} value less than or equal to 10 nanomolar.

160. A method according to Claim 152 wherein the patient is a human.

161. A method for localizing CRF receptors in tissue section samples comprising:

contacting with a sample of tissue a detectably-labelled compound of Claim 3 under conditions that permit binding of the compound to CRF receptors within the sample of tissue;

washing the tissue sample to remove unbound compound; and
detecting remaining bound compound.

162. A packaged pharmaceutical composition comprising a pharmaceutical composition of claim 149 in a container and instructions for using the composition to

D1
cont

treat a patient suffering from an anxiety disorder, a stress-related disorder, or an eating disorder.

09783345-160304